REMARKS

(A) STATUS OF THE APPLICATION

Applicants thank the Examiner for the explanation of rejections in the Non-Final Office Action dated July 02, 2007.

(I) DISPOSITION OF CLAIMS

(i) Claims 1-11 and 13-34 are pending in the application.

(ii) Claim 12 was previously canceled.

(iii) Claims 16-34 are withdrawn under 37 C.F.R. § 1.142(b).

(iv) Claims 1-11, and 13-15 are rejected under 35 U.S.C. § 103(a).

(II) APPLICANTS' ACTION

(ii) Applicants respond to the above rejections.

(B) RESPONSE TO REJECTION UNDER 35 U.S.C. § 103(A)—CLAIMS 1-11 & 13-15

The Examiner has rejected Claims 1-11 and 13-15 under 35 U.S.C. § 103(a) as being obvious over:

(1) WO 01/25316 to Raguse, *et al.* ("Raguse"), in view of

(2) U.S. Pat. No. 6,048,515 to Kresse, *et al.* ("Kresse"), further in view of

(3) U.S. Pat No. 5,922,537 to Ewalt, *et al.* ("Ewalt"), further in view of

(4) U.S. Pub. No. 2002/0120405 to Edwards, *et al.* ("Edwards"), further in view of

(5) Langmuir Journal Publication to Templeton, *et al.* ("Templeton"), and

(6) WO 2001/53478 to Choo, *et al.* ("Choo").

APPLICANTS' RESPONSE

Applicants contend that the Examiner has not met her burden of proving *prima facie* obviousness.

According to the Examiner, Raguse teaches a film comprising cross-linked nanoparticles, wherein the cross-linkers may be proteins. Raguse nanoparticles may comprise gold or iron, a variety of metal oxides, and may be semiconductors. Raguse also teaches that his linkers may have at least two functional groups. Raguse does not specifically teach that his linking protein comprises a member of the pair of glutathione-S-transferase/glutathione not a zinc-finger binding protein. Raguse does teach that his nanoparticles may be coated but does not teach either tiopronin or ethylene glycol coatings.

Raguse claims, but does not exemplify, the use of proteins as cross-linkers for nanoparticles.[1] Raguse generally uses, for example, α,ω-alkane-dithiols or α,ω-alkane-disulfides for cross-linking of the nanoparticles.[2]

Second, Applicants do not disagree that the Raguse nanoparticles are coated. However, they are coated with sodium citrate or octylammonium bromide which do not act as coating components or shielding components. These are ionic species, rendering nanoparticle charge when coated on the surface. Proteins can stick to it by electrostatic interactions. But this is non-specific type of interaction, not the lock-key type of specific interaction found in the subject invention. In other words, the Raguse nanoparticles provide only non-specific binding. For example, bovine serum albumin suggested for use in Raguse's Example 2 would not bind to nanoparticles coated with ethylene glycol oligomers.

In contrast, Applicants have demonstrated that nanoparticles coated with ethylene glycol oligomers actually resist nonspecific binding. Further in contrast to Raguse, protein and nanoparticle interactions in the subject invention are SPECIFIC in nature. Applicants have designed such interactions by choosing protein-ligand binding pairs (see for example, Claim 9).

[1] See Raguse, Example 1 and Claim 17.
[2] See Raguse, Examples 2, & 3, Page 12.

Applicants also note that Raguse does not teach whether the sodium citrate or the octylammonium bromide forms a monolayer coating on the nanoparticles. Furthermore, Raguse relates to forming an array of nanoparticles wherein the nanoparticles are linked to each other. Raguse calls this array a film. The subject invention claims nanoparticles.

Kresse suggests a method for possibly enhancing bifunctional targeting compounds. However, the Kresse bifunctional linker is for example, a small molecule, but not a protein.[3] None of the examples show a bifunctional linker as protein either. The targeting molecules are proteins, but not the bifunctional linkers.

Ewalt mentions the Zinc-finger proteins as a recognition molecule.[4] However, Ewalt mentions the Zinc-finger protein in the context of using DNA as the bifunctional linker. A person skilled in the art differentiates the DNA molecule from a protein, the bifunctional linker in the present invention. Secondly, Ewart links a particle with a protein, whereas the present invention links two nanoparticles.

According to the Examiner, Edwards teaches GST/GSH tags for selectively anchoring proteins to a solid support, specifically to a semiconductor measuring device. However, Edwards demonstrates GST-GSH interaction on a flat substrate surface. As is known to a person of ordinary skill in the art, flat surfaces and nanoparticles differ significantly in their functionalization chemistry. For example, nanoparticle functionalization is usually accomplished during nanoparticle synthesis. A flat surface can be functionalized at any time, generally. What can be demonstrated experimentally on a flat surface cannot be necessarily translated to a nanoparticle surface.

According to the Examiner, Templeton teaches tiopronin monolayers surrounding metallic nanoparticles. However, Templeton relates to water-soluble nanoparticles. It does not relate to a protein-based bifunctional linkers.

[3] See Kresse, Col. 12, Lines 17-30; Col 13, Lines 14-25.
[4] See Ewalt, Col. 7, Lines 39-67.

According to the Examiner, Choo teaches a Zinc-finger protein binding to a sequence 100% identical to the instant SEQ ID NO: 1 and that the protein is particularly useful in biotechnology. However Choo does not anticipate the use of Zinc-finger proteins in materials manipulation.

None of the references provide a suggestion or motivation to combine the references. In fact, the Examiner has to combine six references in an attempt to arrive at claim limitations of the present set of claims. Clearly, the motivation to combine is absent. The fact that six references are required suggests that such combination is an impermissible hindsight reconstruction.

Applicants respectfully submit that all claim limitations are not taught even when said references are combined. Particularly, using a bifunctional linker protein that avoids non-specific binding is not provided even when the references are combined. Thus, there would be no reasonable expectation of success when such references are combined and consequently the first condition of the prima facie case of obviousness is not satisfied.

Because the Examiner has not established a *prima facie* case of obviousness, the present claims are not obvious under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the stated grounds of rejection have been properly traversed, accommodated, or rendered moot and that a complete response has been made to the Non-Final Office Action dated July 02, 2007.

Therefore, Applicants believe that the application stands in condition for allowance with withdrawal of all grounds of rejection. A Notice of Allowance is respectfully solicited.

If the Examiner has questions regarding the application or the contents of this response, the Examiner is invited to contact the undersigned at the number provided.

Should there be a fee due which is not accounted for, please charge such fee to Deposit Account No. 04-1928 (E. I. du Pont de Nemours & Co.).

Respectfully Submitted,

BY:

Date: October 01, 2007

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